```
=> d his

     (FILE 'HOME' ENTERED AT 11:21:26 ON 27 JUN 2002)

     FILE 'HCAPLUS' ENTERED AT 11:21:33 ON 27 JUN 2002
                E ANDO HO?/AU
L1           14 S E8-9
                E BUTLER DO?/AU
L2           77 S E6-8
                E DOZEMAN G?/AU
L3            6 S E4-5
L4            1 S L1 AND L2 AND L3
L5           95 S L1 OR L2 OR L3
L6            1 S L5 AND VASCULAR
L7            1 S L4 OR L6
L8            1 S L5 AND DIABETES
                SELECT L8 1 RN

     FILE 'REGISTRY' ENTERED AT 11:26:02 ON 27 JUN 2002
L9            8 S E1-8

     FILE 'HCAPLUS' ENTERED AT 11:26:12 ON 27 JUN 2002
L10           1 S L8 AND L9

     FILE 'REGISTRY' ENTERED AT 12:01:08 ON 27 JUN 2002
L11             STR

     FILE 'HCAPLUS' ENTERED AT 12:04:46 ON 27 JUN 2002

     FILE 'REGISTRY' ENTERED AT 12:07:20 ON 27 JUN 2002
                SAVE L13 REY617A/A
                SAVE L11 REY617STR/L
L12             STR L11
L13           0 S L12
L14             SCREEN 2008
L15             SCREEN 1838 OR 1992 OR 2016 OR 2026 OR 2021 OR 2043
L16           0 S L12 AND L14 NOT L15
L17             STR L11
L18           0 S L17
L19           0 S L17 AND L14 NOT L15
                E HEXANOIC ACID, 6/CN
                E HEXANOIC ACID, 6,6-OXYBIS/CN
L20          13 S "6,6'-OXYBIS[2,2-DIMETHYL-"
L21           9 S "HEXANOIC ACID, 6,6'-OXYBIS[2,2-DIMETHYL-"
                E HEPTANOIC ACID
                E HEPTANOIC ACID/CN
                E PENTANOIC/CN
L22           1 S E4
L23           2 S "PENTANOIC ACID, 5,5'-OXYBIS[2,2-DIMETHYL-"
L24           1 S "HEPTANOIC ACID, 7,7'-OXYBIS[2,2-DIMETHYL-"
L25          12 S L21 OR L23 OR L24
                SAVE L25 REY617NOM/A
L26          12 S L21 OR L23 OR L24 FULL

     FILE 'HCAPLUS' ENTERED AT 14:54:43 ON 27 JUN 2002
L27          14 S L26
L28           4 S L27 AND (CA OR CALC?)
L29           0 S L27 AND (H2O OR ?HYDRAT?)
```

Inventor search

Searched via nomenclature

HCAPlus via nomenclature search — attached - 14 cits from L26 highlighted on attached printout

FILE 'REGISTRY' ENTERED AT 14:57:59 ON 27 JUN 2002
L30 7 S L26 AND "CALCIUM SALT"
L31 1 S L26 AND "H2O"

highlighted on attached printout

FILE 'HCAPLUS' ENTERED AT 15:00:30 ON 27 JUN 2002
L33 5 S L27 AND PREP?

FILE 'CAOLD' ENTERED AT 15:05:35 ON 27 JUN 2002
L34 0 S L26 — zero hits in CAOLD

FILE 'BEILSTEIN' ENTERED AT 15:05:54 ON 27 JUN 2002
L35 0 S L27 — zero hits in Beilstein

FILE 'REGISTRY' ENTERED AT 15:08:25 ON 27 JUN 2002
L36 0 S L26 AND "?HYDRATE?"
SAVE L26 REY617REG/A
SAVE L30 REY617HCA/A
SAVE L30 REY617REGCA/A
SAVE L31 REY617REGH2O/A

FILE 'HCAPLUS' ENTERED AT 15:12:15 ON 27 JUN 2002
SAVE L27 REY617HCACITS/A REY617HCA/A

Also searched via structure — see d que and search history on following pages.

Nomenclature and structure searches contained the same results (13 hits), except that the nomenclature search retrieved an addnl. hit — so all 14 are included here.

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=> d que 12
L1                STR
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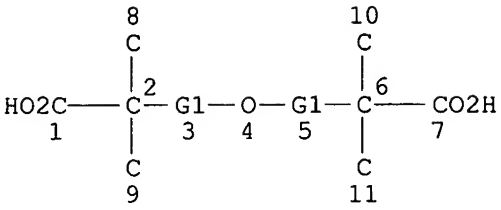


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REP G1=(3-5) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L2  (        11)SEA FILE=REGISTRY SSS FUL L1
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=> d his

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                DEL HAR034HCA/A
                DEL HAR034INV/A
                DEL HAR034MEDL/A
                DEL HAR897INVHCA/A
                DEL HAR944CLU/A

     FILE 'HCAPLUS' ENTERED AT 12:24:36 ON 28 JUN 2002
                ACT REY617MARY/A
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L1               STR
L2  (         11)SEA FILE=REGISTRY SSS FUL L1 - 11 compds in Reg.
L3            13 SEA FILE=HCAPLUS L2 - 13 cit's in HCAPLUS - all were in
               ---------                nomenclature search results
               ACT REY617HCA/A
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L4  (          9)SEA FILE=REGISTRY "HEXANOIC ACID, 6,6'-OXYBIS[2,2-DIMETHYL-"
L5  (          2)SEA FILE=REGISTRY "PENTANOIC ACID, 5,5'-OXYBIS[2,2-DIMETHYL-"
L6  (          1)SEA FILE=REGISTRY "HEPTANOIC ACID, 7,7'-OXYBIS[2,2-DIMETHYL-"
L7  (         12)SEA FILE=REGISTRY L4 OR L5 OR L6
L8            14 SEA FILE=HCAPLUS L7
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L9             1 S L8 NOT L3
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Inventor Search

Reyes 10/018,617

=> d l10 ibib abs hitstr 1

L10 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:564976 HCAPLUS
DOCUMENT NUMBER: 135:122200
TITLE: Preparation and characterization of alcohol and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia, vascular disease and **diabetes**
INVENTOR(S): **Ando, Howard Yoshihisa; Butler, Donald Eugene; Dozeman, Gary Jay**
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

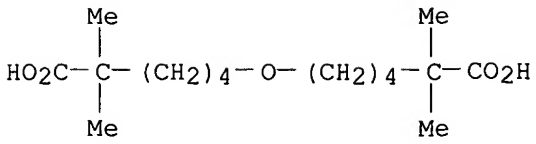
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055078	A1	20010802	WO 2001-IB26	20010111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-177823P P 20000125
OTHER SOURCE(S): MARPAT 135:122200
AB Alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt are prepd. which are cryst. and have the formula -O2CC(CH3)2(CH2)4O(CH2)4CO2-.Ca2+.xR1OH (I; R1 = H, lower alkyl, x = 0-10) [e.g., 6-(5-carboxy-5-methylhexyloxy)-2,2-dimethylhexanoic acid monocalcium salt 1-Pr alc. solvate] and are useful for treating dyslipidemia, **diabetes**, and vascular disease; I-contg. formulations are presented.
IT **209789-08-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(CI 1027; prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and **diabetes**)
RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)

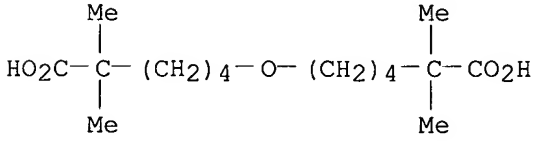
after Priority Date

Searched by Mary Jane Ruhl



IT **351011-22-8P 351011-23-9P 351011-24-0P**
351011-25-1P 351011-26-2P 351011-27-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and **diabetes**)

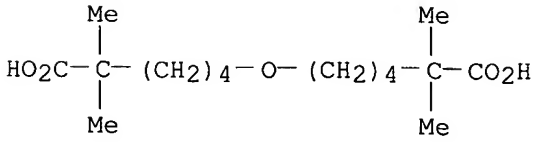
RN 351011-22-8 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1), monohydrate (9CI) (CA INDEX NAME)



RN 351011-23-9 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with ethanol (1:1:1) (9CI) (CA INDEX NAME)

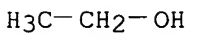
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

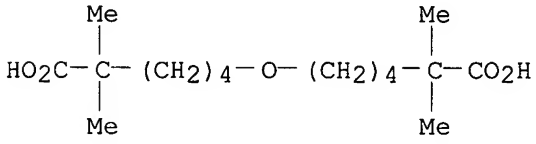
CRN 64-17-5
CMF C2 H6 O



RN 351011-24-0 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with methanol (1:1:1) (9CI) (CA INDEX NAME)

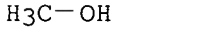
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

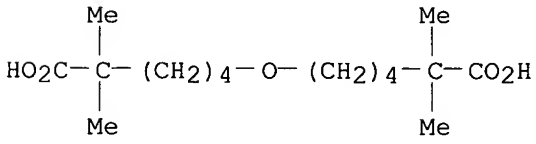
CRN 67-56-1
CMF C H4 O



RN 351011-25-1 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-propanol (1:1:1) (9CI) (CA INDEX NAME)

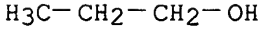
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

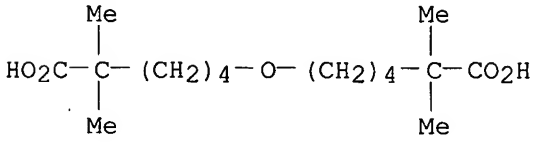
CRN 71-23-8
CMF C3 H8 O



RN 351011-26-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 2-propanol (1:1:1) (9CI) (CA INDEX NAME)

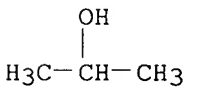
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

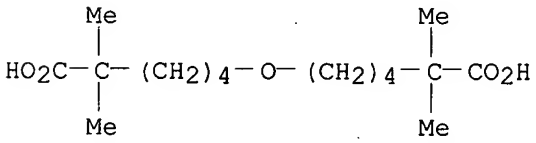
CRN 67-63-0
CMF C3 H8 O



RN 351011-27-3 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-butanol (1:1:1) (9CI) (CA INDEX NAME)

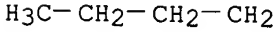
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

CRN 71-36-3
CMF C4 H10 O



IT **1305-78-8**, Calcium oxide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and **diabetes**)
RN 1305-78-8 HCAPLUS
CN Calcium oxide (CaO) (9CI) (CA INDEX NAME)

Ca=O

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 127 ibib abs hitstr 1-14

L27 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:446076 HCAPLUS
TITLE: Process and polymer-based system for controlled-release drug delivery
INVENTOR(S): Fessehaie, Mebrahtu; Ghebre-Sellassie, Isaac; Mollan, Matthew Joseph, Jr.; Mayassi, Monzer Michael; Woldegaber, Haimanot; Dyar, Stephen Craig
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

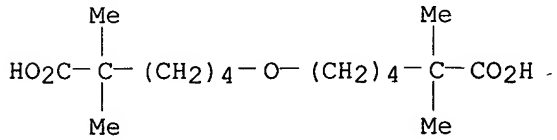
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1213014	A2	20020612	EP 2001-128075	20011127

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-251996P P 20001207

AB A controlled-release dosage form for a pharmaceutically-active agent comprises a core, in which the agent is dispersed, surrounded by a diffusion-limiting sleeve. The agent is released at a zero-order or approx. linear rate because the release rate of the agent will be governed entirely by erosion from exposed core surfaces; the surface area of which does not change substantially during the release process. Such a product may be made by coextruding the core and sleeve material and slicing the extrudate. For example, a compn. for exemplary coating material contained Eudragit RS 95.0% and tri-Et citrate 5.0%, and a compn. for the exemplary core material contained polyvinylpyrrolidone 43.5%, PEG 400 10%, and an active pharmaceutical ingredient, e.g., troglitazone 43.5%. Other active pharmaceutical ingredients used in prepn. of coextruded dosage forms were CI-1017 (an agent useful for treating Alzheimer's disease), CI-1011, an agent useful for regulating lipids in mammals, or CI-1027, an agent useful for treating diabetes and for elevating HDL-cholesterol in mammals.

IT **209789-08-2**, CI-1027
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of polymer-based controlled-release drug delivery system by core/coat coextrusion)
RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)



Ca

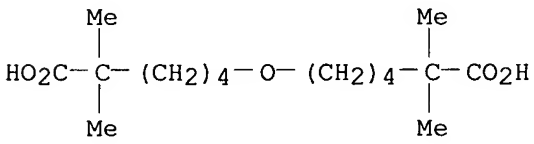
L27 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:71865 HCAPLUS
DOCUMENT NUMBER: 136:112665
TITLE: Treatment of eating disorders using carboxyalkyl ethers
INVENTOR(S): Auerbach, Bruce Jeffrey; Butler, Donald Eugene
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005807	A1	20020124	WO 2001-US16334	20010518

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-218399P P 20000714
OTHER SOURCE(S): MARPAT 136:112665
AB Carboxyalkylethers, e.g. 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid, are useful for treating eating disorders, e.g. obesity.
IT **209789-08-2**, CI 1027
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carboxyalkyl ethers for treatment of eating disorders)
RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)



● Ca

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:903813 HCAPLUS
DOCUMENT NUMBER: 136:15239
TITLE: Carboxyalkyl ether-ACAT inhibitor combinations
INVENTOR(S): Auerbach, Bruce Jeffrey; Zobel, Donna Lee
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001093845	A2	20011213	WO 2001-US14804	20010508

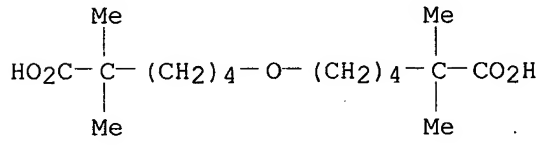
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-210056P P 20000607
OTHER SOURCE(S): MARPAT 136:15239

AB A pharmaceutical compn. comprising (i) a carboxyalkyl ether which lowers triglycerides and LDL and elevates HDL, and (ii) an ACAT inhibitor which improves dyslipidemias in mammals, useful for treating dyslipidemia and ischemic syndromes, and for preventing or delaying the onset of heart attacks is described. A ACAT inhibitor is [(2,4,6-triisopropylphenyl)acetyl]sulfamic acid 6-diisopropylphenyl ester (CI-1011) and a carboxyalkyl ether is 6,6'-oxybis(2,2-dimethylhexanoic acid) or its calcium salt. For example, the lipid modifying and antiatherosclerotic action of CI-1011, CI-1027, and the combination of both compds. was assessed in a rabbit cuff model of atherosclerosis.

IT **209789-08-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CI 1027; carboxyalkyl ether-ACAT inhibitor combinations as antiatherosclerotic and hypocholesterolemic agents)

RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)



● Ca

L27 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798043 HCAPLUS
DOCUMENT NUMBER: 135:339248
TITLE: Antihypertensive agents comprising carboxyalkylethers
INVENTOR(S): Auerbach, Bruce Jeffrey; Hitchcock, Karen Diane; Ryan, Michael John
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080847	A2	20011101	WO 2001-US9088	20010322

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

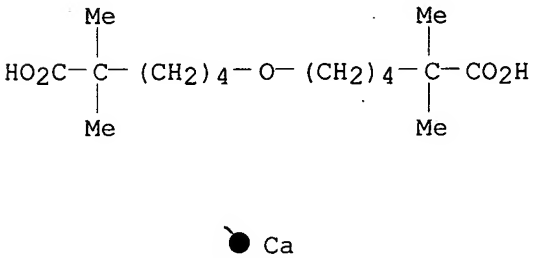
PRIORITY APPLN. INFO.: US 2000-199855P P 20000426
US 2000-242280P P 20001020

OTHER SOURCE(S): MARPAT 135:339248

AB The invention is a pharmaceutical compn. comprising a carboxyalkylether of the formula Y1(R1)(R2)C (CH2)nO(CH2)mC(R3)(R4)Y2 wherein R1, R2, R3, and R4 include alkyl, alkenyl, and alkynyl, m and n are integers from 2 to 9, Y1 and Y2 include COOH, CHO, tetrazole, COOR5 where R5 is alkyl, alkenyl, or alkynyl, or a pharmaceutically acceptable salt thereof, and an antihypertensive agent, said compn. being useful for treating vascular diseases. The invention includes a method of treating hypertension comprising administering a carboxyalkylether. Antihypertensive effect of CI-1027 in combination with quinapril was shown in rats.

IT **209789-08-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CI 1027; antihypertensive agents comprising carboxyalkylethers)

RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)



L27 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:564976 HCAPLUS
DOCUMENT NUMBER: 135:122200
TITLE: Preparation and characterization of alcohol and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia, vascular disease and diabetes
INVENTOR(S): Ando, Howard Yoshihisa; Butler, Donald Eugene; Dozeman, Gary Jay
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055078	A1	20010802	WO 2001-IB26	20010111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

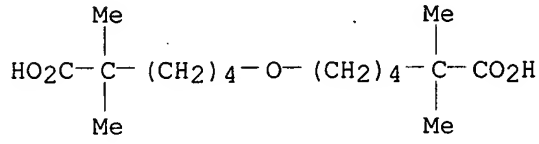
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-177823P P 20000125
OTHER SOURCE(S): MARPAT 135:122200

AB Alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt are prepd. which are cryst. and have the formula -O2CC(CH3)2(CH2)4O(CH2)4CO2-.Ca2+.xR1OH (I; R1 = H, lower alkyl, x = 0-10) [e.g., 6-(5-carboxy-5-methylhexyloxy)-2,2-dimethylhexanoic acid monocalcium salt 1-Pr alc. solvate] and are useful for treating dyslipidemia, diabetes, and vascular disease; I-contg. formulations are presented.

IT **209789-08-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(CI 1027; prepn. and characterization of alc. and water solvates of 6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and diabetes)

RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)

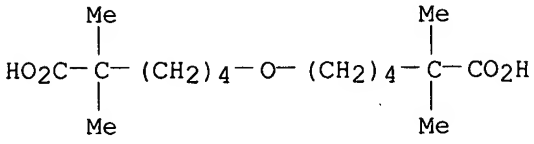


● Ca

IT **351011-22-8P 351011-23-9P 351011-24-0P**
351011-25-1P 351011-26-2P 351011-27-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and characterization of alc. and water solvates of

6-(5-carboxy-5-methyl-hexyloxy)-2,2-dimethylhexanoic acid monocalcium salt for the treatment of dyslipidemia and vascular disease and diabetes)

RN 351011-22-8 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1), monohydrate (9CI) (CA INDEX NAME)



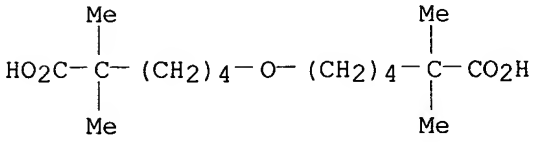
● Ca

● H_2O

RN 351011-23-9 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with ethanol (1:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

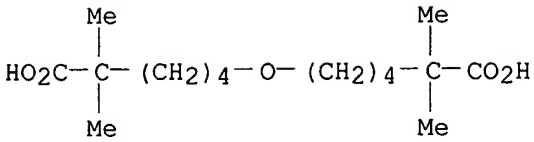
CRN 64-17-5
CMF C2 H6 O

H_3C-CH_2-OH

RN 351011-24-0 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with methanol (1:1:1) (9CI) (CA INDEX NAME)

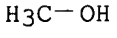
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

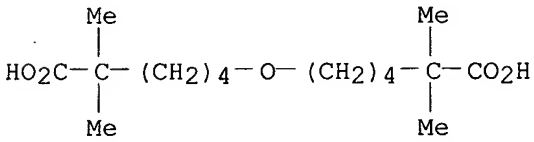
CRN 67-56-1
CMF C H4 O



RN 351011-25-1 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-propanol (1:1:1) (9CI) (CA INDEX NAME)

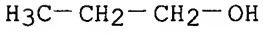
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

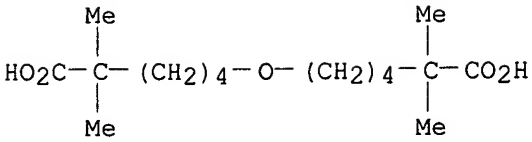
CRN 71-23-8
CMF C3 H8 O



RN 351011-26-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 2-propanol (1:1:1) (9CI) (CA INDEX NAME)

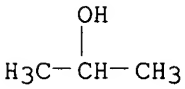
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

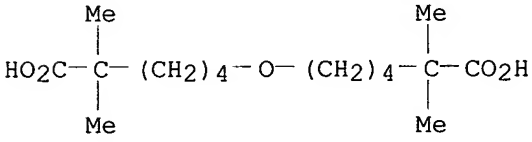
CRN 67-63-0
CMF C3 H8 O



RN 351011-27-3 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt, compd. with 1-butanol (1:1:1) (9CI) (CA INDEX NAME)

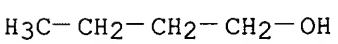
CM 1

CRN 183293-82-5
CMF C16 H30 O5



CM 2

CRN 71-36-3
CMF C4 H10 O



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:725586 HCAPLUS
DOCUMENT NUMBER: 133:291122
TITLE: Ether compounds, compositions, and uses thereof
INVENTOR(S): Dasseux, Jean-louis H.; Oniciu, Carmen D.
PATENT ASSIGNEE(S): Esperion Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059855	A1	20001012	WO 2000-US8788	20000331
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1204626	A1	20020515	EP 2000-921608	20000331
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
US 6410802	B1	20020625	US 2000-540740	20000331

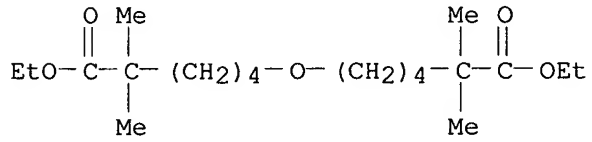
PRIORITY APPLN. INFO.: US 1999-127321P P 19990401
WO 2000-US8788 W 20000331

OTHER SOURCE(S): MARPAT 133:291122

AB The present invention relates to novel ether compds., compns. comprising ether compds., and methods useful for treating and preventing cardiovascular diseases, dyslipidemias, dysproteinemias, and glucose metab. disorders comprising administering a compn. comprising an ether compd. The compds., compns., and methods of the invention are also useful for treating and preventing Alzheimer's Disease, Syndrome X, peroxisome proliferator activated receptor-related disorders, septicemia, thrombotic disorders, obesity, pancreatitis, hypertension, renal disease, cancer, inflammation, and impotence. In certain embodiments, the compds., compns., and methods of the invention are useful in combination therapy with other therapeutics, such as hypocholesterolemic and hypoglycemic agents.

IT **183293-88-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of novel ether compds. and therapeutic and preventive uses thereof)

RN 183293-88-1 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:227499 HCAPLUS
DOCUMENT NUMBER: 132:260690
TITLE: Method using cholesterol-lowering agents for preventing or delaying catheter-based revascularization
INVENTOR(S): Black, Donald Michael

PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

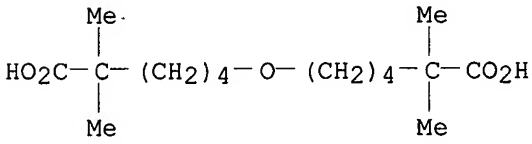
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018395	A1	20000406	WO 1999-US15385	19990708
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9949750	A1	20000417	AU 1999-49750	19990708
EP 1117392	A1	20010725	EP 1999-933763	19990708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9914098	A	20010731	BR 1999-14098	19990708
NO 2001001615	A	20010424	NO 2001-1615	20010329

PRIORITY APPLN. INFO.: US 1998-102457P P 19980930
WO 1999-US15385 W 19990708

AB Aggressively lowering cholesterol in patients suffering from coronary artery disease prevents or delays the need for catheter-based revascularization. A cholesterol-lowering agent, e.g. an HMG-CoA reductase inhibitor such as atorvastatin, is used in an amt. effective to cause an aggressive lowering of LDL cholesterol.

IT **183293-82-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cholesterol-lowering agents for preventing or delaying catheter-based revascularization)

RN 183293-82-5 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:495161 HCAPLUS
DOCUMENT NUMBER: 131:125474
TITLE: Method for treating Alzheimer's disease with agents lowering plasma triglycerides and optional hypocholesterolemic agents
INVENTOR(S): Bisgaier, Charles Larry; Emmerling, Mark Richard
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9938498	A1	19990805	WO 1998-US25495	19981202
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2311356	AA	19990805	CA 1998-2311356	19981202
AU 9916165	A1	19990816	AU 1999-16165	19981202
BR 9814923	A	20001017	BR 1998-14923	19981202
EP 1051161	A1	20001115	EP 1998-960605	19981202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002501887	T2	20020122	JP 2000-529231	19981202
US 2002055529	A1	20020509	US 2001-888592	20010626

PRIORITY APPLN. INFO.: US 1998-72912P P 19980128
WO 1998-US25495 W 19981202
US 2000-554994 A3 20000523

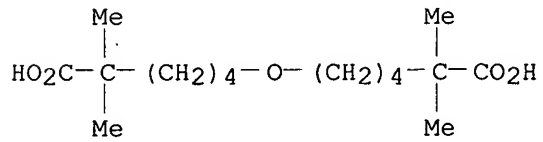
OTHER SOURCE(S): MARPAT 131:125474

AB A method for treating or preventing the onset of Alzheimer's Disease comprises administering to a mammal in need thereof an Alzheimer's Disease-preventing or -treating amt. of a plasma triglyceride level-lowering agent. Optionally, the plasma triglyceride level-lowering agent can be co-administered with a cholesterol level-lowering agent. The relationship between Alzheimer's disease and known risk factors for cardiovascular disease was also studied.

IT **209789-08-2**, CI 1027
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Alzheimer's disease treatment with plasma triglyceride-lowering agents and optional hypocholesterolemic agents)

RN 209789-08-2 HCAPLUS

CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)



● Ca

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:404834 HCAPLUS
DOCUMENT NUMBER: 131:49492
TITLE: Statin-carboxyalkylether combinations for treating vascular diseases
INVENTOR(S): Bisgaier, Charles Larry; Newton, Roger Schofield
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

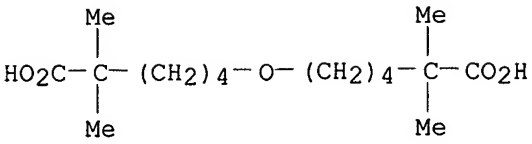
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930704	A1	19990624	WO 1998-US24679	19981120
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304612	AA	19990624	CA 1998-2304612	19981120
AU 9915915	A1	19990705	AU 1999-15915	19981120
BR 9813542	A	20001010	BR 1998-13542	19981120
EP 1045691	A1	20001025	EP 1998-960278	19981120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002508320	T2	20020319	JP 2000-538687	19981120
ZA 9811348	A	19990614	ZA 1998-11348	19981210
NO 2000002966	A	20000609	NO 2000-2966	20000609

PRIORITY APPLN. INFO.: US 1997-69375P P 19971212
WO 1998-US24679 W 19981120

AB The invention is a pharmaceutical compn. comprising a carboxyalkylether which lowers triglycerides and elevated HDL, and a statin which inhibits HMG-CoA reductase, thereby reducing LDL, said compn. being useful for treating vascular diseases. Rats were fed with high cholesterol chow diet and were given 10 mg/kg of 6-6'-oxybis-(2,2-dimethylhexanoic acid calcium salt) and 30 mg/kg of atorvastatin calcium for 14 days. The triglyceride level and HDL/VLDL+LDL was 63 and 2.59 as compared with 118 mg/dL, and 2.59, resp., for the controls.

IT **209789-08-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(statin-carboxyalkylether combinations for treating vascular diseases)

RN 209789-08-2 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, calcium salt (1:1) (9CI) (CA INDEX NAME)



● Ca

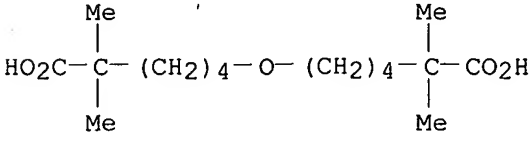
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

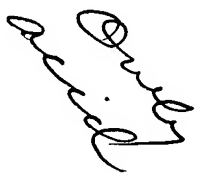
L27 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:124309 HCAPLUS
DOCUMENT NUMBER: 130:305969
TITLE: Automated solid-phase extraction workstations combined with quantitative bioanalytical LC/MS
AUTHOR(S): Huang, N. Helen; Kagel, John R.; Rossi, David T.
CORPORATE SOURCE: Bioanalytical Core Group, Department of Pharmacokinetics and Dynamics, Metabolism, Division of Warner-Lambert, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1999), 19(3-4), 613-620
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An automated solid-phase extn. workstation was used to develop, characterize and validate an LC/MS/MS method for quantifying a novel lipid-regulating drug in dog plasma, i.e. PD 072953. Method development was facilitated by workstation functions that allowed wash solvents of varying org. compn. to be mixed and tested automatically. Precision ests. for this approach were within 9.8% relative std. deviation (RSD) across the calibration range. Accuracy for replicate detns. of quality controls was between -7.2 and +6.2% relative error (RE) over 5-1000 ng mL-1. Recoveries were evaluated for a wide variety of wash solvents, elution solvents and sorbents. Optimized recoveries were generally >95%. A sample throughput benchmark for the method was .apprxeq. 8 min per sample. Because of parallel sample processing, 100 samples were extd. in less than 120 min. The approach has proven useful for use with LC/MS/MS, using a multiple reaction monitoring (MRM) approach.

IT **183293-82-5**, PD 72953
RL: ANT (Analyte); ANST (Analytical study)
(PD 072953 detn. in dog plasma using automated solid-phase extn. workstations combined with quant. bioanal. LC/MS)

RN 183293-82-5 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)





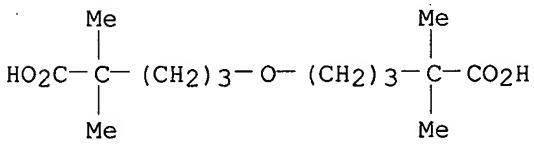
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:374795 HCAPLUS
DOCUMENT NUMBER: 129:62727
TITLE: A novel compound that elevates high density lipoprotein and activates the peroxisome proliferator activated receptor. [Erratum to document cited in CA128:213102]
AUTHOR(S): Bisgaier, Charles L.; Essenburg, Arnold D.; Barnett, Blake C.; Auerbach, Bruce J.; Haubenwallner, Sabine; Leff, Todd; White, Andrew D.; Creger, Paul; Pape, Michael E.; Rea, Thomas J.; Newton, Roger S.
CORPORATE SOURCE: Division of Warner-Lambert Company, Departments of VAscular and Cardiac Diseases, Ann Arbor, MI, 48105, USA
SOURCE: Journal of Lipid Research (1998), 39(6), 1317
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

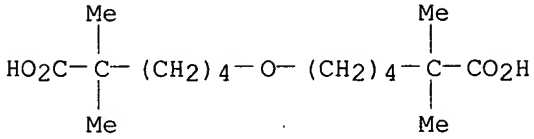
AB In the first column of Table 1, headed "Plasma Determinant," "ApoC-I" should be "ApoC-II.". The cor. Table 1 is given.

IT **171510-89-7**, PD 72660 **183293-82-5**, PD 72953 **183293-83-6**, PD 105726
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PD 72953 and related compds. may reduce plasma triglycerides and apoB-contg. lipoprotein while raising HDL cholesterol via peroxisomal proliferation-activated receptors (Erratum))

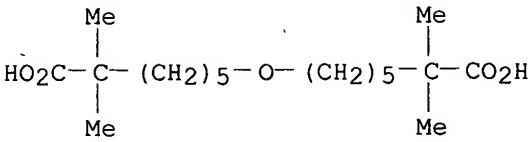
RN 171510-89-7 HCAPLUS
CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 183293-82-5 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 183293-83-6 HCAPLUS
CN Heptanoic acid, 7,7'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



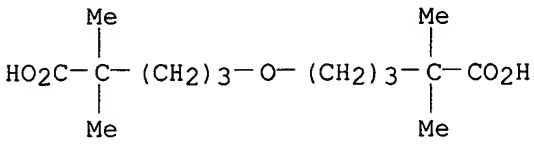
L27 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:61642 HCAPLUS
DOCUMENT NUMBER: 128:213102
TITLE: A novel compound that elevates high density lipoprotein and activates the peroxisome proliferator activated receptor
AUTHOR(S): Bisgaier, Charles L.; Essenburg, Arnold D.; Barnett, Blake C.; Auerbach, Bruce J.; Haubenwallner, Sabine; Leff, Todd; White, Andrew D.; Creger, Paul; Pape, Michael E.; Rea, Thomas J.; Newton, Roger S.
CORPORATE SOURCE: Division of Warner-Lambert Company, Departments of Vascular and Cardiac Diseases, Ann Arbor, MI, 48105, USA
SOURCE: Journal of Lipid Research (1998), 39(1), 17-30
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the current studies, the authors describe the effects of PD 72953 and related compds. on lipoprotein levels in chow-fed male rats. After 2 wk, 10 mg/kg of PD 72953 daily was as effective as 100 mg/kg gemfibrozil for elevating HDL-cholesterol. At 100 mg/kg, PD 72953 further elevated HDL-cholesterol to 232% of control levels, and was assocd. with increased HDL size and plasma apoE (169% of control), despite no change in hepatic apoE mRNA. ApoA-I rose transiently (at 1 wk), but by 2 wk only apoE remained elevated. PD 72953 dose-dependently reduced plasma apoB, VLDL-cholesterol, LDL-cholesterol, and triglyceride. Hepatic apoC-III mRNA redn. paralleled triglyceride lowering. After 1 wk, 30 and 100 mg/kg per day PD 72953 reduced plasma apoC-III levels by 30 and 34%, and triglycerides by 60 and 83%, resp. PD 72953 treatment had no effect on triglyceride prodn. rates; however, 125I-labeled VLDL apoB disappearance was enhanced. The authors compared PD 72953 to a structurally similarly diacid, PD 69405, that also reduced VLDL and LDL, but had no effect on HDL elevation. Compared to PD 72953, PD 69405 further accelerated 125I-labeled VLDL apoB disappearance, decreased triglyceride prodn., and elevated the ratio of post-heparin hepatic to lipoprotein lipase activity. Whole animal studies, transient transfection studies in HepG2 cells, and chimeric receptor studies in kidney 293 cells suggest that PD 72953 is a ligand for the peroxisomal proliferation activated receptor alpha (PPAR.alpha.), and PPAR.gamma.. Overall, PD 72953 may act through a peroxisomal proliferation-activated receptor and result in plasma triglycerides and apoB-contg. lipoprotein redn., while also raising HDL cholesterol. Reduced apoC-III may allow triglyceride-rich remnants to more efficiently bind and present substrate to peripheral tissue lipoprotein lipase, and therefore allow enhanced shedding of remnant phospholipid surface for HDL prodn.

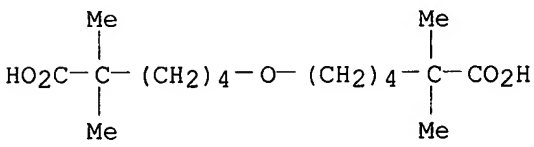
IT **171510-89-7**, PD 72660 **183293-82-5**, PD 72953
183293-83-6, PD 105726
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PD 72953 and related compds. may reduce plasma triglycerides and apoB-contg. lipoprotein while raising HDL cholesterol via peroxisomal proliferation-activated receptors)

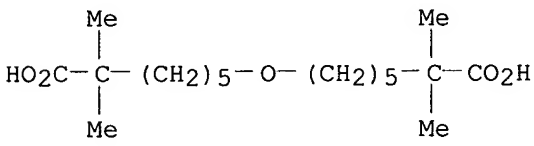
RN 171510-89-7 HCAPLUS
CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 183293-82-5 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 183293-83-6 HCAPLUS
CN Heptanoic acid, 7,7'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



L27 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:689457 HCAPLUS
DOCUMENT NUMBER: 125:328104
TITLE: Preparation of terminal carboxy or tetrazole group-containing dialkyl ethers as anticholesteremics and antidiabetics
INVENTOR(S): Bisgaier, Charles Larry; Creger, Paul Leroy; Saltiel, Alan Robert; Tafuri, Sherrie Rae
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630328	A1	19961003	WO 1996-US1639	19960205
W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT				
US 5648387	A	19970715	US 1995-409780	19950324

CA 2215233	AA	19961003	CA 1996-2215233	19960205
AU 9647768	A1	19961016	AU 1996-47768	19960205
AU 692359	B2	19980604		
EP 820428	A1	19980128	EP 1996-903794	19960205
EP 820428	B1	20000510		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
CN 1182415	A	19980520	CN 1996-193500	19960205
JP 11502532	T2	19990302	JP 1996-529342	19960205
AT 192732	E	20000515	AT 1996-903794	19960205
ES 2148733	T3	20001016	ES 1996-903794	19960205
PL 181673	B1	20010831	PL 1996-322407	19960205
CZ 289556	B6	20020213	CZ 1997-2922	19960205
ZA 9602275	A	19960930	ZA 1996-2275	19960320
US 5750569	A	19980512	US 1997-805533	19970225
US 5756544	A	19980526	US 1997-806582	19970225
US 5783600	A	19980721	US 1997-806580	19970225
FI 9703713	A	19970924	FI 1997-3713	19970917
NO 9704397	A	19971120	NO 1997-4397	19970923

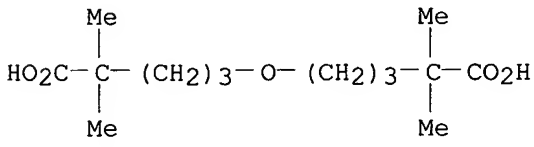
PRIORITY APPLN. INFO.: US 1995-409780 A 19950324
WO 1996-US1639 W 19960205

OTHER SOURCE(S): MARPAT 125:328104

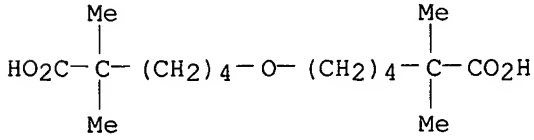
AB The title compds. Y1(R1)(R2)C(CH2)nO(CH2)mC(R3)(R4)Y2 [I; R1-R4 = alkyl, alkenyl, alkynyl; Y1, Y2 = CO2H, CHO, tetrazole, (un)substituted carboxylate ester; m, n = 2-9], which lower Lp(a) and triglycerides and elevate HDL-cholesterol, useful for treating vascular diseases and noninsulin-dependent diabetes mellitus, are prepd. and I-contg. formulations presented. Thus, isobutyric acid was reacted with 4,4'-dichlorobutyl ether in the presence of (MeHC)2 and NaH, producing 6,6'-oxybis(2,2-dimethylhexanoic acid), m.p. 49-51.degree., which demonstrated anticholesteremic activity.

IT **171510-89-7P 183293-82-5P 183293-83-6P**
183293-87-0P 183293-88-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of terminal carboxy or tetrazole group-contg. dialkyl ethers as anticholesteremics and antidiabetics)

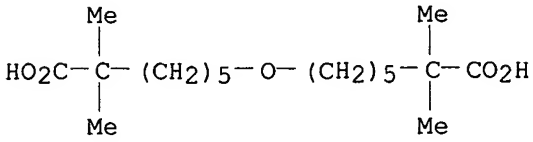
RN 171510-89-7 HCAPLUS
CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



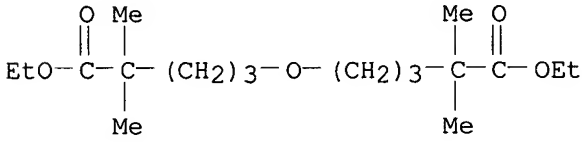
RN 183293-82-5 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



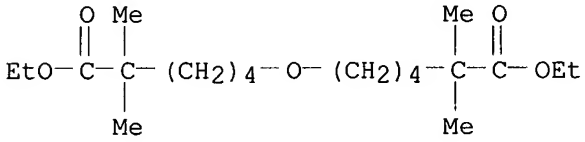
RN 183293-83-6 HCAPLUS
CN Heptanoic acid, 7,7'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)



RN 183293-87-0 HCAPLUS
CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl-, diethyl ester (9CI) (CA INDEX NAME)



RN 183293-88-1 HCAPLUS
CN Hexanoic acid, 6,6'-oxybis[2,2-dimethyl-, diethyl ester (9CI) (CA INDEX NAME)



L27 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:803901 HCAPLUS
DOCUMENT NUMBER: 124:29095
TITLE: Synthesis of 5,5,10,10-tetramethyl-1-oxacyclotridecane-6,7,8,9-tetrone - on the mechanism of the Rubottom reaction
AUTHOR(S): Gleiter, Rolf; Staib, Michael; Ackermann, Uwe
CORPORATE SOURCE: Organisch-Chemisches Inst. Univ. Heidelberg, Heidelberg, D-69120, Germany
SOURCE: Liebigs Ann. (1995), (9), 1655-61
CODEN: LANAEM; ISSN: 0947-3440
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:29095
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The synthesis of 5,5,10,10-tetramethyl-1-oxacyclotridecane-6,7,8,9-tetrone (12) was achieved via a multistep procedure involving an oxidn. known as the Rubottom reaction. The key intermediates were the dialdehyde (I), the

diacid (II), the cyclic diketone (III) and the bis(silyl enol ether) (IV). The oxidn. of IV with mCPBA yielded two diastereomeric hydroxy ketones , V (R = .alpha.-OH, .beta.-OH), the ratio of which depends strongly on the solvent used. This result combined with the isolation of the diepoxide (VI) gives an insight into the stereochem. of the Rubottom reaction.

IT **171510-89-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of tetramethyl-1-oxacyclotridecanetetrone and mechanism of Rubottom reaction)

RN 171510-89-7 HCAPLUS

CN Pentanoic acid, 5,5'-oxybis[2,2-dimethyl- (9CI) (CA INDEX NAME)